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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/699,338	10/31/2003	Birgit Sehested Hansen	6443.500-US	2536

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EXAMINER	
ZHANG, NANCY L	
ART UNIT	**PAPER NUMBER**
1614	

DATE MAILED: 12/15/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

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Office Action Summary	Application No.	Applicant(s)	
	10/699,338	HANSEN ET AL.	
	Examiner	Art Unit	
	Nancy L. Zhang	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 November 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-43* is/are pending in the application.

4a) Of the above claim(s) *3 and 8-13* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,4-7 and 14-17* is/are rejected.

7)☒ Claim(s) *1, 2 and 17* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *2 sheets*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's election of Group II, claims 1-2, 4-11 and 13-43 along with 4-hydroxy-3-nitroacetophenone for treating obese type II diabetes as the elected species, in the reply filed on November 10, 2006, is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Claims 3 and 12 are withdrawn from consideration because they are not directed to the elected invention.

Claims 8-11, 13 and 18-43 are withdrawn from consideration because they are not directed to the elected species.

Claims 1-2, 4-7 and 14-17 are considered.

Specification

The applicant is advised to correct "60/xxx,xxx" to "60/516,588" on page 1, line 6 of the specification.

Claim Objections

Claims 1-2 and 17 are objected to because of the following informalities:

Regarding claims 1 and 2, the incorporation by reference to "Assay (I)" is improper.

Regarding claim 17, the use of Markush group is improper. The phrase "selected from" should be changed to "selected from the group consisting of". The components in

a Markush group should be linked by commas and the conjunction of "and" should be used to link the last two components of the Markush group.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-2, 4-7 and 14-17 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1-2 are rejected as failing to define the invention in the manner required by 35 U.S.C. 112, second paragraph. The claim(s) are narrative in form and replete with indefinite and functional or operational language. The recitation of a compound having a slope "of a value less than the value for the slope calculated from the above equation..." is unclear. The limitation "in Assay (I)" is indefinite because there is insufficient antecedent basis for this limitation in the claim.

Claims 1-2, 4-7 and 14-17 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential elements, such omission amounting to a gap between the elements. See MPEP § 2172.01. The omitted elements are: the subject of which the compound is administered to.

Lack Written Description Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-2, 4-7 and 14-16 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The invention of claims 1-2, 4-7 and 14-16 is directed to a method of treatment by increasing mitochondrial respiration comprising administering a compound having a specific value calculated from an equation or a prodrug thereof.

Regarding claims 1-2, 4-7 and 14-15, the recitation of the claims encompasses an extremely broad range of compounds without any structural limitation other than the characterization of the compounds having a slope calculated from the equation of claim 1. The specification discloses some example compounds and formulas and teaches how to calculate the slope value for a compound of the formulas using measurements from Assay (I). No structure connection is established between the slope value and the compounds. The disclosure does not meet the written description provision of 35 USC § 112, 1st Paragraph. The specification provides insufficient written description to support the genus encompassed by the claims to include any compound having a slope value calculated from the equation of claim 1.

Regarding the recitation of "a prodrug" in claims 1-2, 4-7 and 14-16, this recitation encompasses a broad range of compounds. The specification does not provide any structural limitation other than that "prodrug" includes biohydrolyzable amides and biohydrolyzable esters. Nor does the specification teach how to screen for a prodrug of a compound. An amide or an ester of a compound only defines a chemical bond in the compound and therefore encompasses an unlimited range of compounds. The specification provides insufficient written description to support the genus encompassed by the claims to include a prodrug of the claimed compounds.

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is not claimed." (See page 1117). The specification does not "clearly allow persons of ordinary skilled in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116).

In the instant case, a skilled artisan cannot envision the detailed chemical structure of the encompassed chemicals or their prodrugs, regardless of the characterization of having a slope calculated from the equation. Adequate written description requires more than a mere statement that it is part of the invention and reference to potential compounds. The chemical itself is required. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993) and Amgen Inc. V. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016. Finally, University of California v. Eli Lilly and Co., 43 USPQ2d 1398, 1404, 1405 held that:

...To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." Lockwood v. American Airlines, Inc., 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997); In re Gosteli, 872 F. 2d 1008, 1012, 10 USPQ2D 1614, 1618 (Fed. Cir. 1989) ("[T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." Lockwood, 107 F.3d at 1572, 41 USPQ2D at 1966.

Therefore, claims 1-2, 4-7 and 14-16 do not meet the written description provision of 35 USC § 112, 1st Paragraph. Applicant is reminded that Vas-Cath makes clear that the written description provision of 35 USC § 112 is severable from its enablement provision (see page 1115).

Scope of Enablement Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-2, 4-7 and 14-17 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a compound having effects of

increasing glucose utilization, does not reasonably provide enablement for any treatment or treating all of the disease conditions encompassed by the claims using any compound. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. 112, first paragraph, have been described in In re Wands, 8 USPQ2d 1400 (Fed. Cir. 1988). Among these factors are: (1) the nature of the invention; (2) the state of the prior art; (3) the relative skill of those in the art; (4) the predictability or unpredictability of the art; (5) the breadth of the claims; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary. When the above factors are weighed, it is the examiner's position that one skilled in the art could not practice the invention without undue experimentation.

The instant invention relates to a method of treating a disease condition benefiting from an enhancement of mitochondrial respiration by the administration of the claimed compound(s).

With respect to enable of treatment of "a disease condition benefiting from an enhancement of mitochondrial respiration", "a compound having a slope calculated from an equation" or "a prodrug thereof",

The relative skill of those in the art of pharmaceuticals and the unpredictability of the pharmaceutical art is very high. In fact, the courts have made a distinction between

mechanical elements function the same in different circumstances, yielding predictable results, chemical and biological compounds often react unpredictably under different circumstances. Nationwide Chem. Corp. v. Wright, 458 F. supp. 828, 839, 192 USPQ 95, 105(M.D. Fla. 1976); Aff'd 584 F.2d 714, 200 USPQ 257 (5th Cir. 1978); In re fischer, 427 F.2d 833, 839, 166 USPQ 10, 24(CCPA 1970). Thus, the physiological activity of a biological compound is considered to be an unpredictable art and the physiological or pharmaceutical activity of treating "a disease condition benefiting from an enhancement of mitochondrial respiration" is an unpredictable art.

The claims are very broad due to the vast number of possible diseases conditions that are described as being "a disease condition benefiting from an enhancement of mitochondrial respiration" including "obesity, atherosclerosis, hypertension, diabetes, type 2 diabetes, impaired glucose tolerance, dyslipidemia, coronary heart disease, gallbladder disease, osteoarthritis, cancer, endometrial cancer, breast cancer, prostate cancer, colon cancer and the maintenance of a weight loss". Furthermore, the claims are further complicated by the compounds having characteristic of "a slope value calculated from the equation" or "prodrugs thereof". The scope of the claimed invention covers "any disease condition benefiting from an enhancement of mitochondrial respiration", "any compound having a slope value calculated from the equation" or "prodrugs thereof" that are known to exist and those that may be discovered in the future, for which there is no enablement provided.

Although some known chemical uncouplers that have activities in increasing the metabolic rate may be useful in treating obesity, it is not known yet that a single

underlying mechanism ties together all of the seemingly unrelated manifestation of the disease conditions encompassed (for example, obesity, gallbladder disease and breast cancer). There is no demonstrated correlation or sufficient evidence in the specification or incorporated by reference that increased glucose utilization would be able to treat all the diseases encompassed. Therefore, the skilled artisan would turn to undue amount of trial and error to find out which disease or condition would be response to the administration of sad compounds.

The specification discloses the effects of increased glucose utilization (Figures 1-3) using the compounds that have a slope value calculated from an equation. However, the specification fails to provide how to make and screen "compound having a slope value calculated from the equation" or "prodrugs thereof" encompassed by the instant claims without undue amount of experimentation. As discussed in preceding comments, in the instant case, only a limited number of "a compound capable of increase glucose utilization" (no example or no definition of "prodrugs thereof") is disclosed in the specification, thereby the specification fails to provide sufficient working examples. It is noted that these examples are neither exhaustive, nor define the class of compounds required. The instant claims read on any compounds having "a slope value calculated from the equation" or "prodrugs thereof", necessitating an exhaustive search for the embodiments suitable to practice the claimed invention. Applicants fail to provide information sufficient to practice the claimed invention, absent undue experimentation.

As discussed in preceding comments, to practice the instant invention to the claimed scope, applicant would have to (i) make or screen numerous potentially suitable

compounds characterized as "having a slope value calculated from the equation" or "prodrugs thereof", (ii) undergo assays to find out which compounds are able to exert the desired pharmacological activity, and then (iii) extrapolate the test and result to the claimed therapeutic utility. In other words, the instant invention necessitates for the skilled artisan to undergo an exhaustive search for the embodiments suitable to practice the claimed invention.

Given the breadth, the disparate nature of compounds that is presently claimed, the highly unpredictable state of the art where many specific differences or different physicochemical properties are existed among unrelated structural compounds or even structurally related compounds, the limited number of working examples and the insufficient amount of guidance present in the specification, one of ordinary skill in the art would have to undergo an undue amount of experimentation to practice the claimed invention.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

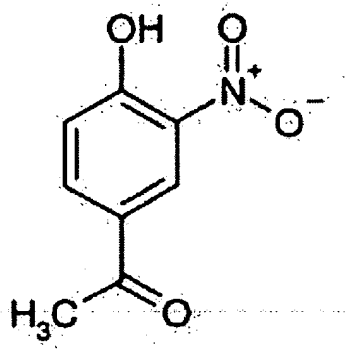
> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein

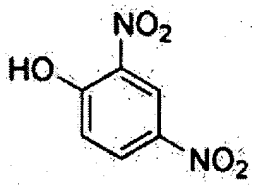
were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-2, 4-7 and 14-17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bachynsky (US Patent 4,673,691, issue date: Jun. 16, 1987) in view of Batt et al. (US Patent 5,593,994, issue date: Jan. 14, 1997) and Rink et al. (US Patent 5,739,106, issue date: Apr. 14, 1998) as applied to claims 4-7.

The invention of claims 1-2, 4-7 and 14-17 are directed to a method comprising the administration of a compound having a slope calculated from an equation as defined in claim 1. Further limitation include that the method is for treating a disorder such as Type II diabetes or obesity in a patient (claims 2 and 4-7). A compound for the treatment is the elected species of 4-hydroxy-3-nitroacetophenone having the following structure:



Bachynsky teaches a method of inducing weight loss in a patient comprising administering 2,4-dinitrophenol (DNP) (column 6, lines 20-22) having the following structure:



The prior art teaching differs from the instant invention in that (i) the prior art compound has a nitro group at position 4 whereas the compound of the instant invention has an aceto group at position 4 and (ii) the prior art does not disclose that the obese patient has type II diabetes.

However, the base structure of the prior art compound 2,4-dinitrophenol is the same as the base structure of 4-hydroxy-3-nitroacetophenone of the instant invention and the physiological activities are analogous. In addition, Batt et al. disclose compounds for treatment where the substitute groups on the benzene ring can be nitro or aceto (column 49, line 39). Therefore, the substitution of a nitro group with an aceto group on the benzene ring is obvious. One having ordinary skill in the art would have been motivated to substitute a nitro group of the prior art compound with an aceto group with the expectation that the substitution would not significantly alter the analogous properties of the compound due to close structural similarity of the compounds. See In re Grunwell, 203 USPQ 1055.

With respect to the patient population for treatment in claims 4-7 where the patient who is obese is suffering from type II diabetes, Rink et al. disclose that obesity

and type 2 diabetes are associated in both clinical and epidemiological studies (column 1, lines 29-31) and that weight reduction is often recommended as the first course of action for patients suffering from Type II diabetes (column 1, lines 42-45). Therefore, one having ordinary skill in the art would have been motivated to practice a weight reduction method of treatment to treat obese patient who is suffering from Type II diabetes.

Therefore, it would have been obvious to someone of ordinary skill in the art at the time of the instant invention to practice the treatment of Bachynsky in view of Rink et al. with compound modifications in view of Batt et al. to result in the practice of the instant invention with a reasonable expectation of success.

The recitation of the compound having a slope calculated from an equation as defined in claims 1-2, 4-7 and 14-17 is merely a characterization of the compound and therefore does not limit the claims.

With respect to the recitation of "increasing mitochondrial respiration" in the claims, when the same compound is administered to treat the same patient population, the mechanism of action of "increasing mitochondrial respiration" is expectedly present.

Regarding the recitation of claim 14, since there is no extra active step in the method of treatment for conducting the Assay, the compound being a chemical uncoupler as defined is merely a characterization of the compound and therefore does not limit the claim.

Regarding the recitation of claim 15, since the nitro group of the prior art compound is the same nitro group of the instant compound, the fact that the nitro group

is a cation is merely a characterization of the compound and therefore does not limit the claim.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nancy L. Zhang whose telephone number is (571)-272-8270. The examiner can normally be reached on Mon.- Fri. 8:30am - 5:00pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel can be reached on (571)-272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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